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INTRODUCTION

Progress in understanding inflammatory and autoimmune diseases of the central nervous system

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This issue of *Seminars in Immunopathology* is devoted to the topic of inflammatory and autoimmune diseases of the central nervous system (CNS). As editors, we are gratified that a panel of distinguished expert colleagues kindly accepted our invitation to contribute an article, each covering an essential aspect of the overall topic. Taken together, the articles cover a broad spectrum of neuroimmunology and neuroinflammation.

In the first article, Wei Hu and Claudia F. Lucchinetti discuss the neuropathological spectrum of CNS inflammatory demyelinating diseases. The authors emphasize the emerging heterogeneity of these disorders, with multiple sclerosis (MS) being the most common but by no means only the disease in this category. They also provide us with an update on the exciting new developments in neuromyelitis optica, a disorder which has recently been redefined by the presence of autoantibodies against the aquaporin-4 water channel. The second article, authored by Monika Bradl and Hans Lassmann, focuses on progressive MS, the "step-child of MS therapeutics." The authors demonstrate that also in progressive MS, inflammation is the driving force for CNS injury, and they present plausible explanations why it is so difficult to treat progressive forms of MS.

In the third article, Klaus Dornmair, Edgar Meinl, and Reinhard Hohlfeld discuss novel approaches for identifying target antigens of autoreactive human B and T cells. Whereas many antigens have shown encephalitogenic properties in animal models, it has been difficult to identify the target antigens of pathogenic immune reactions in human diseases. New techniques allow the isolation of individual tissue-infiltrating B and T cells, so that their clonotypical antigen-specific receptors can be reconstructed from single cells. The reconstructed antigen-specific receptors are then expressed in living cell lines, which can be used in the search for unknown target antigens.

In the next article, merits and shortcomings of animal models of MS are critically discussed in detail by Bettina Schreiner, Frank L. Heppner, and Burkhard Becher. Various experimental autoimmune encephalomyelitis (EAE) models have greatly contributed to our current understanding of MS pathogenesis, albeit it has been difficult to bridge the gap between EAE and MS research. The most recent generation of EAE models make extensive use of genetic engineering methods, such as transgenic and knockout techniques, allowing detailed studies of various aspects of immunopathogenesis. Special emphasis is placed on models elucidating the role of newly emerging subsets of autoimmune T cells, including TH17 cells and regulatory T cells (Treg).

Britta Engelhardt and Lydia Sorokin provide firsthand insight into the intricate workings of one of the most essential areas of neuroinflammation, the blood–brain and blood–cerebrospinal fluid barriers. The authors discuss the structure of the blood–brain barrier under physiological conditions and emphasize how changes of its function become crucially important in pathological conditions. The blood–brain barrier is also a key site for therapeutic intervention, as recently evidenced by the approval of the therapeutic monoclonal antibody natalizumab, which is directed against alpha-4-beta-1-integrin and inhibits the influx of autoaggressive T cells into the CNS.

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Lisa Walter and Harald Neumann then authoritatively discuss the role of microglia in neuronal degeneration and regeneration, emphasizing that microglia has a double-sided nature because it can both mediate neuroprotection and neurotoxicity.

Neil J. Scolding provides an overview on CNS vasculitis, describing different subtypes of vasculitis and discussing diagnostic and therapeutic approaches.

In the last article of this issue, Jan Bauer and Christian G. Bien consider different kinds of encephalitis associated with epilepsy: Rasmussen encephalitis, paraneoplastic encephalitis and certain forms of nonparaneoplastic encephalitis.

We hope that the readers are as excited as we are about this unique collection of articles covering a wide spectrum of current basic and clinical neuroimmunology. We would like to thank all authors and co-authors for their excellent contributions and, last but not least, would like to express our gratitude to the editorial staff of Springer for competently supporting us in preparing this issue.